REMARKS

Reconsideration of the patentability of applicants' claims is requested respectfully.

Status of the Claims

The Examiner's Action addresses all of applicants' elected claims, namely Claims 1, 3, 6, 7 and 27 to 38. No claims have been amended or cancelled. Accordingly, there is presented for the Examiner's consideration Claims 1, 3, 6, 7, and 27 to 38.

Summary of the Examiner's Rejections

In response to applicants' Supplemental Reply of December 23, 2002, the Examiner has not reasserted the rejections in his Action of June 3, 2002, but has asserted new rejections which include the citation of two references not of record previously.

Claims 1, 6, 7, 27 to 31, 34, 35, 37 and 38 have been rejected under 35 U.S.C. § 103 (a) as being anticipated over the knowledge of one of ordinary skill in the art in view of the combined disclosures of U.S. Patent No. 5,004,610 to Osborne *et al.* (hereafter "the Osborne reference") and U.S. Patent No. 5,914,282 to Dunshee et al. (hereafter, "the Dunshee reference"), each newly cited.

Claims 3, 32, 33, and 36 have been rejected under 35 U.S.C. § 103 (a) as being obvious over the knowledge of one of ordinary skill in the art in combination with the combined disclosures of the Osborne and Dunshee references and of previously cited U.S. Patent No. 5,316,759 to Rose et al. (hereafter "the Rose reference").

Reconsideration of the Examiner's rejections is requested respectfully.

Summary of Applicants' Invention

Applicants' invention is summarized in the Reply that was filed on March 15, 2002. As reflected in applicants' Claims 1 and 27 and as described in detail in the March 15 Reply, two features which distinguish applicants' transdermal patch over the prior art are: (i) a solid silicone adhesive layer which contains a normally volatile drug (for example, nicotine) and which is a source in the patch of the drug; and (ii) a solid acrylic adhesive layer which underlies (viewed from the area of skin contact) the silicone adhesive layer and which is in diffusional contact therewith. The resins comprising these layers and the positioning of the layers in the patch are critical to the effective manufacture of the patch and to its successful functioning.

As to the drug-containing layer, volatile drug in the patch is contained initially in the layer of silicone adhesive which is highly soluble in a high vapor pressure solvent, for example, hexane. In forming applicants' patch, a layer containing the volatile drug is formed from a solution of the volatile drug, the silicone adhesive, and the high vapor-pressure solvent by casting a film of the solution and evaporating the solvent. The solvent evaporates readily at a relatively low temperature, that is, at a temperature at which loss of the volatile drug is minimized or avoided during the drying process which leads to formation of the solid layer of the drug-containing silicone adhesive. In contrast, the use of an adhesive (as the drug-containing adhesive) which is not highly soluble in a high vapor-pressure solvent and which requires the use of a solvent that has a relatively low vapor pressure (thus, requiring the use of relatively high "evaporating" temperatures) would result in the loss of a substantial amount of the volatile drug during the manufacturing process.

As to the acrylic adhesive layer which underlies the drug-containing silicon adhesive layer, the rate of drug diffusion through the acrylic adhesive is slower than the diffusion rate through a silicone adhesive. Accordingly, there is a controlled diffusion of the drug from the acrylic adhesive layer to the skin over a sustained period of time.

The discussion which follows shows clearly that none of the references of record renders obvious this combination of resin layers in a patch which contains a volatile drug. The disclosures of the references cited by the Examiner in the rejections are summarized below.

Summary of the Disclosures of the References

The disclosure of each of the references first made of record in the present Action is summarized below. The previously cited Rose reference is summarized in applicants' Reply of March 15, 2002 and is not repeated herein.

U.S. Patent No. 5,004,610 to Osborne *et al.*

Although newly cited, the Osborne reference issued from an application which is the parent of the application that issued as U.S. Patent No. 6,165,497 to Osborne et al. on which the Examiner based art rejections in the previous Action. With the exception of minor formatting differences and the claims, the specifications of the two Osborne patents are identical.

The Osborne reference discloses a transdermal patch for the administration of nicotine comprising (col. 3, lines 35-62) the following elements:

> (a) a nicotine-containing layer which functions as a source of nicotine for the patch; (b) a nicotine flux rate-controlling layer; and (c) a skin-contacting adhesive layer through which a drug administered by the patch diffuses (col. 4, lines 67 to 68).

The nicotine-containing layer described in the Osborne reference is a viscous mass which is capable of either "flowing or oozing" (col. 3, line 50-51) or which has "sufficient viscosity to maintain its structural integrity" (col. 3, line 51-54) and which comprises, in preferred form, "... nicotine dissolved in a solvent..." (col. 5, lines 7 to 9).

The Osborne reference discloses also that the matrix of the nicotine-containing layer is preferably anhydrous and can comprise "...natural and synthetic rubbers or other polymeric materials, thickened mineral oils or silicone fluids or petroleum jelly..." (col. 6, lines 32-37). Preferably, the nicotine-containing layer of the Osborne patch comprises ethylene vinyl acetate (EVA) copolymer (col. 6, lines 36-41).

The Osborne reference does not disclose the use of a silicone resin as a constituent of an adhesive layer which contains nicotine and which is a source of nicotine in the patch.

The nicotine flux rate-controlling layer described in the Osborne patch comprises either a "dense polymer film ...[permeable]... to nicotine" (col. 6, lines 47 to 55) or an oil-filled, microporous, drug-impermeable polymer membrane as described in U.S. Patent Nos. 3,792,494 to Zaffaroni and 4,031,894 to Urquhart *et al.*, (see Osborne at col. 7, lines 18 to 24).

The Osborne reference does not disclose the use of an acrylic resin as the nicotine flux rate-controlling layer.

The skin-contacting adhesive layer which underlies the rate-controlling layer in the Osborne patch is described as a material which is known in the art for use in a transdermal patch and through which nicotine can diffuse such that the adhesive "does not constitute a significant permeation barrier to the passage of nicotine" (col. 7, lines 24-36), for example, silicone-based adhesives such as, for example, Dow Corning X7-2920 (col. 7, lines 54-55).

In summary, the Osborne reference that is, the primary reference, does not describe either a solid silicone adhesive layer which is a source of the drug in the patch or an underlying solid acrylic adhesive layer which is in diffusional contact with the silicone adhesive layer.

U.S. Patent No. 5,914,282 to Dunshee *et al.*

The Dunshee reference describes an adhesive composite sheet for use with a wound dressing or for use as an adhesive tape for skin contact. The composite sheet comprises a porous backing layer which has laminated thereto a polymeric barrier layer which, in turn, has adhered thereto a skin-contacting adhesive layer. Prior to application to the skin, the skin-contacting adhesive layer has adhered thereto a release liner. Optionally, for use in a wound dressing, an adsorbent pad may reside between a portion of the adhesive layer and the release liner. The Dunshee reference describes broadly, for skin contact, acrylic-based adhesives which can include polymers prepared by copolymerizing one or more ethylene moiety-containing compounds with one or more of

an acrylic acid compound and an acrylic acid ester compound, including isooctylacrylate and ethyl(hexyl)acrylate compounds.

There is no disclosure whatsoever in the Dunshee reference respecting the use of a silicone-based adhesive or of the use of a drug. Indeed, the Dunshee reference does not disclose a transdermal patch or any device having an adhesive layer through which a drug diffuses.

Discussion and Traversal of the Examiner's § 103 Rejections

It is submitted respectfully that the Examiner's rejections are not sound and, accordingly, should be withdrawn because, among other reasons, the Examiner's rejections are based on an inaccurate view of the disclosure of the primary reference, namely, the Osborne reference.

The §103 Rejections Based on the Osborne
Reference in Combination with the Dunshee Reference

The Examiner has presented two §103 rejections which are based either in whole or in part on the Examiner's assertion that applicants' patch is *prima facie* obvious in view of the combined disclosures of the Osborne and Dunshee references. As pointed out above, applicants' generic claims (Claims 1 and 27) define a patch which comprises a silicone adhesive layer, which is a source in the patch of a drug, and, underlying and in diffusional contact therewith, an acrylic adhesive layer. The Examiner's position is based on the mistaken view that the Osborne reference discloses a patch that has a nicotine reservoir which comprises a silicone adhesive and nicotine (that is, a layer which

contains nicotine and is the source of nicotine in the patch). In support of this view, the Examiner refers to Example I of the Osborne reference (col. 7, lines 51 to 55).

In fact, however, Example I of the Osborne reference does not describe a silicone adhesive layer which contains nicotine and is the source of nicotine in the patch. Example I describes a patch having a "nicotine reservoir layer"which contains not silicone resin, but instead an ethylene/vinyl acetate (EVA) copolymer. The silicone adhesive referred to in Example I is in the skin-contacting adhesive layer which underlies the "nicotine reservoir layer".

Although applicants acknowledge that Example I might have been written more clearly, it is, nevertheless, abundantly clear that the silicone adhesive (Dow Corning X7-2920) referred to in Example I is not in the "nicotine reservoir layer", but is in the skin-contacting adhesive layer of the Osborne et al. delivery device. This construction of the device is consistent with the Osborne et al. detailed description of their device. In this regard, the Examiner's attention is directed to the Osborne reference, Column 7, lines 25 to 35, where it is disclosed that a silicone adhesive which is an amine-resistant adhesive can be used as the skin-contacting adhesive layer ("5" in Figures 1 and 2). Furthermore, such adhesive is not disclosed by Osborne et al. as an example of an adhesive that can be used in the make-up of the "nicotine reservoir layer" (see Column 6, lines 30 to 41 of the Osborne reference). Consistent with Example I, this section of the Osborne reference discloses that EVA copolymer is a preferred constituent for use in the reservoir layer.

The §103 Rejections of Claims 1, 6, 7, 27-31, 34, 35, 37 and 38
Based On The Combination Of The Osborne And Dunshee References

The Examiner's §103(a) rejections of Claims 1, 6, 7, 27 to 31, 34, 35, 37 and 38 which are based on the combined disclosures of the Osborne and Dunshee references are

traversed. As explained above, the Osborne reference does not describe a patch which includes either a solid silicone adhesive layer that contains a drug and that is a source of the drug in the patch nor a solid acrylic adhesive layer which underlies and is in diffusional contact therewith. The Examiner has not cited any references, including the Dunshee reference, nor provided any evidence of a level of skill in the art at the time of the invention which would lead one to modify the patch described in the Osborne reference to yield applicants' patch. Inasmuch as the Osborne et al. patch and applicants' patch have materially different constructions and there is no teaching or even a remote suggestion respecting the modification of the Osborne patch to yield a patch of applicants' construction, it is requested respectfully that the Examiner's §103(a) rejections based on the disclosure of the Osborne reference in combination with the Dunshee reference be withdrawn.

The §103 Rejection of Claims 3, 32, 33, and 36 Based on the Osborne Reference in Combination With the Dunshee and the Rose References.

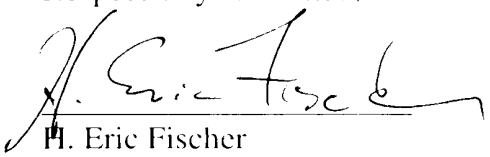
The Rose reference, summarized in applicants' Reply to the Office Action of October 15, 2001, discloses no single structural or functional feature that corresponds to a structural or functional feature of applicants' development. Summarizing from applicants' earlier Reply, the Rose reference discloses a transdermal patch having, as a source of a drug, either a liquid solution containing the drug or a liquid drug in a neat form contained in a pouch formed between a liquid-impermeable backing layer and a liquid-permeable skin-contacting layer. The disclosure of the Rose reference, when combined with the disclosure of the Osborne and Dunshees reference, does not result in a patch having a solid silicone adhesive layer which contains a volatile drug and is a source of the drug in the patch nor a solid acrylic adhesive layer underlying and in diffusional contact with the solid silicone adhesive layer. The record contains no

evidence that the ordinary level of skill existing in the art at the time of applicants' invention would lead a skilled artisan to a modify the patches described by the combined references to yield applicants' patch. Accordingly, it is requested respectfully that the aforementioned Examiner's §103 rejection of Claims 3, 32, 33, and 36 be withdrawn.

In view of the foregoing, applicants' request respectfully that the Examiner allow the application in an early and favorable Action.

This Reply is accompanied by a Petition for a one-month extension of the reply period, that is, from October 8, 2003 to November 8, 2003 (a Saturday).

Respectfully submitted,



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